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Attitudes must change if we are to avoid another Mediator° scandal

● **The Mediator° (*benfluorex*) scandal provides an opportunity to try to redress the balance in the relationship between pharmaceutical companies and the public authorities responsible for medicines, in Europe and elsewhere.**

● **If we are to avoid another scandal like Mediator°, attitudes of healthcare professionals, patients, and experts or authorities in the drug field also need to change. This article makes a number of suggestions as to how the current system could be improved.**

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In addition to the specific failures highlighted by the Mediator° (*benfluorex*) scandal, it revealed wider shortcomings in the drug regulatory system in both France and Europe, and their harmful consequences in terms of human lives. It drew media and public attention to other drugs that should have long since been withdrawn from the market or should never have been authorised in the first place. It illustrated inadequacies in the regulation of drugs and the pharmaceutical industry; in the priorities and the decision-making process of the drug regulatory agencies, the French national health system and the government ministries concerned; in the initial and continuing education of healthcare professionals, particularly in clinical pharmacology and public health.

The strong reactions elicited by the Mediator° scandal in France will perhaps lead to a lasting improvement in the laws, rules and practices of the pharmaceutical industry and regulatory agencies.

But in addition to demonstrating the need for tighter regulation of the drug market, this scandal also shows that a number of attitudes that are frequently held by healthcare professionals, patients, and experts or authorities in the drug field, in Europe and elsewhere, need to be challenged and changed: healthcare professionals who give insufficient weight to scientific evidence in their decision-making; excessive faith placed in rapid, certain progress; paternalism and authoritarianism among healthcare professionals, experts and authorities; a fatalistic attitude towards the adverse effects of treatments; blurring of roles and unhealthily close links between the experts or authorities within pharmaceutical companies and regulatory agencies.

Hope, a double-edged sword

Uncertainty is omnipresent in medicine. Diagnostic and therapeutic procedures, including drug treatments, are often probability-based. This uncertainty leaves plenty of room for wishful thinking among all parties in the medical and pharmaceutical field.

Patients consult healthcare professionals because they hope to obtain relief, care or even a cure. When doctors and pharmacists prescribe or recommend a particular treatment, they hope to cure or improve their patients' condition. One of the motivations of scientists and pharmaceutical companies is their hope of developing a new drug with a favourable harm-benefit balance. One of the incentives for public agencies and policymakers in their decision to authorise a drug, reimburse a high proportion of its cost, or price it affordably is the hope of helping patients get access to a new therapeutic advance.

Hope that is sometimes betrayed. Hope alone does not cure patients, and it can be deliberately or accidentally betrayed: by definition, this is what distinguishes doctors from charlatans.

Patients feel that their hopes and trust have been betrayed when their doctor has not taken the best course of action, made a mistake or did not tell them the truth.

This is the ambiguity of the placebo effect, where the hope of improvement is based on deception if the healthcare professional presents the prescribed treatment as more effective than it is..

As a result of the limitations of healthcare professionals' knowledge, their words and actions are dictated by their hope of curing the patient rather than grounded in scientific evidence. Healthcare professionals need to be informed about the current state of knowledge, in order to recognise when they are straying into the realm of blind hope and great uncertainty, or even delusion. It is a common scenario with new drugs, when there is scant information, sometimes based on assumptions or supposed mechanisms of action. And this information is often biased because it was ▶▶

► provided by pharmaceutical companies.

The dangers of unfounded hope. This is where medicine can border on charlatanism: when the healthcare professional knows very little about a drug, but speaks about it with conviction, based only on the hope of doing some good (or appearing well informed). But convictions do not prevent disasters. Hope does not prevent a drug from being no more effective than placebo, or of having serious adverse effects. Taking these risks is based on hope, and the patient is always the first to lose.

Sometimes, when all else fails and the prognosis is grim, all that healthcare professionals and patients have left is hope, with no basis in scientific evidence. It can then be tempting to "do something" anyway; but this should not make the situation worse, as is sometimes the case in elderly patients with dementia or in certain cancers, for example.

Action is tempting but sometimes harmful. Outside the context of terminal illness, many healthcare professionals and patients seem to share the conviction that "something must be done" about any symptom or discomfort, and that an appropriate drug must exist.

The attitude that it is always better to act, and that there is a drug for everything, results in potentially inappropriate use of drugs, especially when the adverse effects of a treatment cause more harm than the natural course of the disease or disorder.

Practitioners should resist the desire or need to act at all costs.

Progress, a fruitful but risky endeavour

Healthcare professionals' and patients' hope that every new drug represents a therapeutic advance is due in large part to their ignorance of the regulations governing the authorisation of new drugs: new drugs are only required to be superior to placebo or at best "non-inferior" to similar drugs.

This wishful thinking is also due to widespread faith in technological progress, which is often considered inevitable, necessary and limitless.

In the healthcare field, progress in terms of healthy life expectancy does have limits. Claiming that medicine will one day enable everyone to live to the age of 100 and still be in good health is grounded only in faith.

Progress is slow and uncertain, the best drugs can be very old. Blind faith in progress is likely to lead to a step backwards in healthcare. In therapeutic disciplines where the standard drugs are old, belief in constant progress can result in considering these older drugs to be "out of date". They are then replaced by new drugs that better embody the idea of "innovation", yet their therapeutic value is purely hypothetical and their unknown effects could in time prove harmful to patients.

Progress is necessary in many healthcare disciplines, but in practice it is often much slower and more modest than hoped. It is risky to use progress as a pretext to devalue the past.

Resist paternalism and authoritarianism

In medical and nursing practices, hospitals and community pharmacies, healthcare professionals question patients about various aspects of their lives, including their personal and private life. They prescribe the care they consider most suitable, and sometimes advise them on their diet, sex life, education, much as a parent would a child...

But, like an authoritarian parent, healthcare professionals sometimes make decisions without asking or taking into account the patient's point of view. Healthcare professionals sometimes truly believe that they know better than patients what is good for them, and think they have the right not to disclose the whole truth and to withhold information.

Withholding the truth breeds distrust of the healthcare system. Authoritarian behaviour results in substandard care and loss of patient trust: when healthcare professionals conceal the adverse effects of a drug or the limitations of a diagnosis; when drug regulatory agencies refuse to disclose information in their possession, refuse to justify their decisions, and shroud their proceedings in secrecy; when health authorities hide the limitations of a screening programme, exaggerate the dangers of an epidemic, or downplay the adverse effects of a vaccine.

Authoritarian healthcare professionals decide unilaterally that a drug's adverse effects are acceptable given the expected clinical benefit, without taking into account the patient's point of view, preferences or living conditions.

Many patients feel let down when they realise that a healthcare professional in whom they placed their trust has withheld important information. Not disclosing the potential adverse effects of a treatment to patients, under the pretext that it is best not to "scare" them, is common behaviour. It amounts to treating patients like children while denying them the opportunity of adequately protecting themselves.

And when patients discover they have been exposed to preventable adverse effects, their distrust can extend to the whole healthcare system, not only the specific drug or healthcare professional concerned.

Attitudes towards adverse effects are too often fatalistic

Medicine is in essence a fight against the inevitability of ill health, accidents and disease. Healthcare professionals try to be supportive and sympathetic, to correct defects or deficiencies, reduce suffering, prevent or cure disease, prolong life and alleviate disability.

Once they are committed to a course of action, hoping that it will be effective, healthcare professionals sometimes adopt a fatalistic attitude towards its adverse effects: the expression "*all drugs have adverse effects*" sometimes results in trivialising rather than preventing adverse effects.

The adverse effects are too often downplayed, overshadowed by a blind focus on benefits.

A fatalistic attitude towards adverse effects among healthcare professionals results from an underdeveloped culture of patient safety, inadequate application of the principle of "first, do no harm". Fatalism is harmful when drugs with a better harm-benefit balance are available, when the benign nature of the problem makes exposure to any risk of serious adverse effects unacceptable, or when satisfactory, safe, non-drug alternatives exist. It is harmful even when no better treatment option exists, because there are often ways to prevent or reduce the risk of adverse effects.

Blurring of the roles between pharmaceutical companies and regulators

Scandals in which adverse effects are too long unrecognised or downplayed, drugs are authorised too hastily, or a drug's price or reimbursement rate is higher than its therapeutic value warrants, result from inadequate defence of the public interest and excessive influence of the pharmaceutical industry. Public and private interests do not coincide, even though some are common to both. Public authorities need to keep a firm hold on the reins, preventing them from weakening or abandoning their duties.

If a healthcare agency or its staff seeks to defend both the health of patients and that of the pharmaceutical industry,

more or less explicitly and consciously, this blurring of roles is frequently not in the patients' best interests, because pharmaceutical companies are closer to the centre of power.

It would be better to replace such tacit agreement on compromise solutions with debates between the concerned parties, each clearly stating its interests and defending them passionately or even fiercely. Is open, explicit debate not a better way of airing and defending opposing interests than an implicit, vague consensus, reached behind closed doors?

Unhealthily close links between the various experts or authorities

The Mediator° scandal and the debates it provoked made the general public aware of the concept of conflicts of interest: because influential individuals work both on behalf of the pharmaceutical industry and for the drug regulatory agency, they are simultaneously judging and being judged. Beyond the concept of conflicts of interest, drug regulatory agency decisions are also influenced by the unhealthily close links between their staff or experts and industry representatives.

Tacit compromise, possibly unconscious, but always kept secret, is a standard method of decision-making in these committees and working groups. They do not have to disclose the details of their discussions, their arguments, the evidence they used, or their votes. Especially when some internal rule or usual practice states that the goal is to reach "consensus". How many potential whistleblowers have been gagged by the pursuit of consensus?

Too much biased consensus. Consensus is even harder to break when the decision-makers, representing healthcare administrators, pharmaceutical companies, government, health professionals and even patients, have all known each other for a long time. They often obtained the same qualifications from the same universities, belong to the same socio-economic classes and the small circle of experts, etc. It would take real courage and motivation to dare to speak out in such meetings.

A decisive element for ensuring that cliquish, consensual decision-making does not become the norm, is the transparency of the meetings. But frequent and regular change in the various representatives who sit on the committees is also essential, extending recruitment to other circles and other countries.

At a different level, the same people can successively occupy positions of power in government ministries, pharmaceutical companies, drug regulatory agencies, then return to the pharmaceutical industry. This revolving door is often detrimental to patients and beneficial to the pharmaceutical industry. Going back and forth between these different positions is unacceptable.

The truth, the whole truth

In addition to the necessary improvements to the practices of the pharmaceutical industry and regulators, the Mediator° scandal will only lead to lasting improvements if healthcare professionals, patients, experts and authorities change some of their attitudes: basing their actions on critical appraisal of scientific evidence; making shared, transparent decisions; paying more attention to adverse effects; avoiding the blurring of roles and unhealthily close links between those in authority.

Through the Mediator° scandal, *Prescrire* has become better known, achieved greater prominence, and has been able to promote some of the guiding principles it has upheld for the past 30 years, reflected in the following suggestions:

– to endeavour to give as small a role as possible to hope that is not grounded in solid evidence: to reach conclusions on the basis of evidence, i.e. after examining the facts, as opposed to assumptions and wishful thinking;

– to tell the truth to patients and the public: drug regulatory agencies and pharmaceutical companies should make all information publicly available;

– to tell the whole truth to patients who want to know: the evidence as well as any uncertainties;

– to criticise those who do not fulfil their role, whether they be politicians, pharmaceutical companies, drug regulatory agencies, educators, healthcare professionals, or patient advocacy groups;

– not to take a fatalistic view of the adverse effects of healthcare, but rather to constantly draw attention to them;

– not to seek consensus or close ties with other stakeholders in the healthcare system, in particular with its expert advisors or those in authority;

– to firmly uphold values and evidence, at the risk of sometimes being portrayed as overly dogmatic. This choice derives not from condemning the actions of specific individuals (within the pharmaceutical industry, drug regulatory agencies, etc.) but from seeking effective treatments, for the benefit of patients. It sometimes sets us against other societal stakeholders who have different or even opposing interests, some of which are very powerful.

As of 2011, The French edition of *Prescrire* is 30 years old and has 35 000 subscribers. Many healthcare professionals have long identified with its values and rely every day on the information it publishes to improve their professional practice and avoid similar tragedies.

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European Medicines Agency: complete transparency needed

● **Trial protocols and raw data.**

The experience of two medical research scientists from the Nordic Cochrane Centre in Copenhagen shows that, as of 2011, the European Medicines Agency (EMA) still lacks transparency and works first and foremost for the pharmaceutical industry (1).

The EMA obstructs access to clinical data. In 2007, while the EMA was examining the marketing authorisation applications for *rimonabant* (formerly marketed under the brand name Acomplia°) and *orlistat* (Xenical°, Alli°), the two scientists requested the complete clinical trial reports and protocols of 15 placebo-controlled trials of these two drugs (1).

The scientists wanted to check the robustness of the results and measure any discrepancy between the published and unpublished data. The information requested *"was important for patients because anti-obesity pills are controversial. The effect on weight loss in the published trials is small, and the harms are substantial (…), and most of the drugs have been deregistered for safety reasons"* (1).

After several refusals from the EMA's director, who went as far as demanding evidence that the requested documents were of major public interest, the ▶▶